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DATE: Friday, March 18, 2005 Printable Copy Create Case

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DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L21	l20 same l15	68	L21
L20	l13 with lysine	677	L20
L19	l13 with polylysine	393	L19
L18	L17 with l13	37	L18
L17	modified	1621054	L17
L16	L15 same L14	15	L16
L15	dna or nucleic or gene or polynucleotide	412038	L15
L14	L13 same L11	412	L14
L13	L8 with L1	1004	L13
L12	L11 same L6	31	L12
L11	combination	3271661	L11
L10	L8 same L6	43	L10
L9	L8 same L7	101435	L9
L8	L7 or L3	138486	L8
L7	arginine or positive charge	101435	L7
L6	L5 with L1	624	L6

L5	transpo$ or deliv$ or transfe$	4142171	L5
L4	L3 with L2	7	L4
L3	lysine or polylysine	88412	L3
L2	hexa with histidine	3368	L2
L1	polyhistidine or (poly with histidine)	7422	L1

END OF SEARCH HISTORY

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L4: Entry 7 of 7 File: DWPI Jul 5, 2001

DERWENT-ACC-NO: 2001-425579
DERWENT-WEEK: 200380

TITLE: Pharmaceutical composition useful for delivering therapeutic agent for treating diseases, comprises a peptide characterized with specified number of amino acids and a specified percentage of histidine residues

INVENTOR: MIXSON, A J

PATENT-ASSIGNEE:

ASSIGNEE	CODE
MIXSON A J	MIXSI

PRIORITY-DATA: 1999US-173576P (December 29, 1999), 2001US-0018103 (November 5, 2001), 2002US-0131909 (April 25, 2002)

Search Selected Search ALL Clear

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200147496 A1	July 5, 2001	E	064	A61K009/14
AU 200122812 A	July 9, 2001		000	A61K009/14
EP 1242052 A1	September 25, 2002	E	000	A61K009/14
US 20030045465 A1	March 6, 2003		000	A61K038/10
US 20030165567 A1	September 4, 2003		000	A61K038/16

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
WO 200147496A1	December 20, 2000	2000WO-US34603	
AU 200122812A	December 20, 2000	2001AU-0022812	
AU 200122812A		WO 200147496	Based on
EP 1242052A1	December 20, 2000	2000EP-0986605	
EP 1242052A1	December 20, 2000	2000WO-US34603	

EP 1242052A1		WO 200147496	Based on
US20030045465A1	December 20, 2000	2000WO-US34603	
US20030045465A1	November 5, 2001	2001US-0018103	
US20030165567A1	December 29, 1999	1999US-173576P	Provisional
US20030165567A1	December 20, 2000	2000WO-US34603	CIP of
US20030165567A1	November 5, 2001	2001US-0018103	CIP of
US20030165567A1	April 25, 2002	2002US-0131909	

INT-CL (IPC): A61 K 9/127; A61 K 9/14; A61 K 38/08; A61 K 38/10; A61 K 38/16; A61 K 48/00; C07 K 14/00; C12 N 15/00; C12 N 15/63; C12 N 15/88

RELATED-ACC-NO: 2003-865520

ABSTRACTED-PUB-NO: WO 200147496A
BASIC-ABSTRACT:

NOVELTY - A pharmaceutical agent delivery composition (I) comprises a transport polymer (II) comprising a peptide (P), characterized as having at least 10 amino acid residues, where at least 10% of the amino acid residues are histidine, and a pharmaceutical agent is associated with (II).

DETAILED DESCRIPTION - The molecular structure of (P) is linear, with the proviso that the entire sequence of the peptide cannot be described by the formula (XHHX)n or (XHXH)n, where H is histidine, X is a hydrophobic amino acid, and n is an integer at least 4, and the peptide does not comprise a hexa-peptide having the sequence (His)6, unless and at least 10% of the remaining amino acid residues of the peptide are histidine, or is branched, with a backbone peptide of 1 or more amino acid residues and at least one peptide branch of 1 or more amino acid residues covalently attached to a side-group of an amino acid residue of the backbone peptide, with the proviso that each peptide branch consists of a single histidine residue only if the backbone peptide does not consist solely of lysine residues.

An INDEPENDENT CLAIM is also included for producing (I).

ACTIVITY - Antisickling; antianemic; nootropic; cardiant; cytostatic; hemostatic; antiparkinsonian; antiarthritic; anti-HIV; antidiabetic; virucide.

MECHANISM OF ACTION - Gene therapy. No supporting data given.

USE - (I) is useful for delivering a pharmaceutical agent to the interior of a cell, by removing cells from a subject, contacting the cells with (I), and administering the cell to the subject after contacting the cell with (I) (claimed). (I) is useful for treating adenosine deaminase deficiency, purine nucleoside phosphorylase deficiency, chronic granulomatous disease with defective p47phox, sickle cell with HbS, beta -thalassemia due to inadequate production of beta -hemoglobin, Faconi's anemia, familial hypercholesterolemia due to a defective low-density lipoprotein receptor, alpha 1-antitrypsin deficiency, phenylketonuria due to phenylalanine hydroxylase deficiency, ornithine transcarbamylase deficiency, apolipoprotein E deficiency, hemophilia A and B due to factor VIII and IX deficiency, respectively, muscular dystrophy due to dystrophin, laminin-2, or sacroglycans mutations, cystic fibrosis due to CFTR mutations, Parkinson due to tyrosine hydroxylase deficiency, retinitis pigmentosa, lysosomal storage disease (i.e., mycopolysaccharide type 1, Hunter, Hurler and Gaucher), diabetic retinopathy, human immunodeficiency virus disease, virus infection, acquired

anemia, cardiac and peripheral vascular disease and arthritis.

CHOSEN-DRAWING: Dwg.0/18

TITLE-TERMS: PHARMACEUTICAL COMPOSITION USEFUL DELIVER THERAPEUTIC AGENT TREAT DISEASE COMPRISE PEPTIDE CHARACTERISTIC SPECIFIED NUMBER AMINO ACID SPECIFIED PERCENTAGE HISTIDINE RESIDUE

DERWENT-CLASS: B04 D16

CPI-CODES: B04-C01; B04-C01B; B04-E01; B12-M05; B14-A02; B14-A02B1; B14-C09; B14-F01; B14-F06; B14-H01; B14-J01A; B14-J01A3; B14-J01A4; B14-S03; B14-S04; D05-C01; D05-C11; D05-H10; D05-H12;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
Fragmentation Code
F014 F019 F521 F599 H1 H101 H183 J0 J014 J1
J171 J3 J373 M280 M312 M315 M323 M332 M343 M349
M371 M381 M393 M423 M431 M510 M523 M530 M540 M720
M782 M904 M905 N153 P210 P421 P444 P517 P522 P617
P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A4JPBK A4JPBT A4JPBQ A4JPBM A4JPBP

Chemical Indexing M1 *02*
Fragmentation Code
F014 F019 F521 F599 H1 H101 H183 J0 J014 J1
J171 J3 J373 M280 M311 M312 M315 M321 M323 M332
M342 M343 M349 M371 M381 M393 M423 M431 M510 M523
M530 M540 M720 M782 M904 M905 N153 P210 P421 P444
P517 P522 P617 P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A4JPFK A4JPFT A4JPFQ A4JPFM A4JPFP

Chemical Indexing M1 *03*
Fragmentation Code
F014 F019 F521 F599 H1 H101 H183 J0 J014 J1
J171 J3 J373 M280 M311 M312 M315 M321 M323 M332
M342 M343 M349 M371 M381 M393 M423 M431 M510 M523
M530 M540 M720 M782 M904 M905 N153 P210 P421 P444
P517 P522 P617 P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A4JPRK A4JPRT A4JPRQ A4JPRM A4JPRP

Chemical Indexing M1 *04*
Fragmentation Code
F014 F019 F521 F599 H1 H101 H183 J0 J014 J1
J171 J3 J373 M280 M311 M312 M315 M321 M323 M332
M342 M343 M349 M371 M381 M393 M423 M431 M510 M523
M530 M540 M720 M782 M904 M905 N153 P210 P421 P444
P517 P522 P617 P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A4JPXK A4JPXT A4JPXQ A4JPXM A4JPXP

Chemical Indexing M1 *05*
Fragmentation Code
F014 F019 F521 F599 H1 H101 H183 J0 J014 J1

J171 J3 J373 M280 M311 M312 M315 M322 M323 M332
M342 M343 M349 M371 M381 M393 M423 M431 M510 M523
M530 M540 M720 M782 M904 M905 N153 P210 P421 P444
P517 P522 P617 P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A4JPZK A4JPZT A4JPZQ A4JPZM A4JPZP

Chemical Indexing M1 *06*
Fragmentation Code
F014 F019 F521 F599 H1 H101 H183 J0 J014 J1
J171 J3 J373 M280 M312 M315 M323 M332 M343 M349
M371 M381 M393 M423 M431 M510 M523 M530 M540 M720
M782 M904 M905 N153 P210 P421 P444 P517 P522 P617
P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A4JQ1K A4JQ1T A4JQ1Q A4JQ1M A4JQ1P

Chemical Indexing M1 *07*
Fragmentation Code
M423 M431 M530 M540 M720 M782 M904 M905 N153 P210
P421 P444 P517 P522 P617 P812 P815 P816 P820 P823
P922 Q233
Specfic Compounds
A4JQ3K A4JQ3T A4JQ3Q A4JQ3M A4JQ3P

Chemical Indexing M1 *08*
Fragmentation Code
F014 F019 F521 F599 H1 H101 H183 J0 J014 J1
J171 J3 J373 M280 M312 M315 M323 M332 M343 M349
M371 M381 M393 M423 M431 M510 M523 M530 M540 M720
M782 M904 M905 N153 P210 P421 P444 P517 P522 P617
P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A4JQMK A4JQMT A4JQMQ A4JQMM A4JQMP

Chemical Indexing M1 *09*
Fragmentation Code
F014 F019 F521 F599 H1 H101 H183 J0 J014 J1
J171 J3 J373 M280 M311 M312 M315 M321 M323 M332
M342 M343 M349 M371 M381 M393 M423 M431 M510 M523
M530 M540 M720 M782 M904 M905 N153 P210 P421 P444
P517 P522 P617 P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A4JRGK A4JRGT A4JRGQ A4JRGM A4JRGP

Chemical Indexing M1 *10*
Fragmentation Code
M423 M431 M720 M782 M905 N153 P210 P421 P444 P517
P522 P617 P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A00H1K A00H1T A00H1Q A00H1M A00H1P

Chemical Indexing M1 *11*
Fragmentation Code
M423 M431 M782 M905 P210 P421 P444 P517 P522 P617
P812 P815 P816 P820 P823 P922 Q233
Specfic Compounds
A00H3K A00H3T A00H3Q A00H3M

Chemical Indexing M1 *12*

```
    Fragmentation Code
    M423 M431 M782 M905 P210 P421 P444 P517 P522 P617
    P812 P815 P816 P820 P823 P922 Q233
    Specfic Compounds
    A00NSK A00NST A00NSQ A00NSM

Chemical Indexing M1 *13*
    Fragmentation Code
    M423 M431 M782 M905 P210 P421 P444 P517 P522 P617
    P812 P815 P816 P820 P823 P922 Q233
    Specfic Compounds
    A012PK A012PT A012PQ A012PM

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C2001-128774
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L10: Entry 23 of 43 File: PGPB Jul 5, 2001

PGPUB-DOCUMENT-NUMBER: 20010006817
PGPUB-FILING-TYPE: new-utility
DOCUMENT-IDENTIFIER: US 20010006817 A1

TITLE: CELL DELIVERY COMPOSITIONS

PUBLICATION-DATE: July 5, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
PACK, DANIEL W.	CHAMPAGNE	IL	US	
PUTNAM, DAVID A.	CAMBRIDGE	MA	US	
LANGER, ROBERT S.	NEWTON	MA	US	

APPL-NO: 09/ 251783 [PALM]
DATE FILED: February 17, 1999

CONTINUED PROSECUTION APPLICATION: CPA

RELATED-US-APPL-DATA:
Application is a non-provisional-of-provisional application 60/075272, filed February 19, 1998,

INT-CL: [07] C12 Q 1/68, C07 H 21/02, C07 H 21/04, C12 N 15/00, A61 K 31/70, A01 N 43/04, C12 P 21/06, C12 P 19/34, C07 K 2/00, C07 K 4/00

US-CL-PUBLISHED: 435/440; 514/44, 435/6, 435/69.1, 435/91.1, 435/455, 435/456, 435/458, 435/325, 530/350, 530/300, 536/23.1
US-CL-CURRENT: 435/440; 435/325, 435/455, 435/456, 435/458, 435/6, 435/69.1, 435/91.1, 514/44, 530/300, 530/350, 536/23.1

REPRESENTATIVE-FIGURES: NONE

ABSTRACT:

The present invention provides improved cell delivery compositions. In particular, the invention provides biocompatible endosomolytic agents. In a preferred embodiment, the endosomolytic agents are also biodegradable and can be broken down within cells into components that the cells can either reuse or dispose of. Preferred endosomolytic agents include cationic polymers, particularly those comprised of biomolecules, such as histidine, polyhistidine, polylysine or any combination thereof. Other exemplary endosomolytic agents include, but are not limited to, other imidazole containing compounds such as vinylimidazole and histamine. More particularly preferred are those agents having multiple proton acceptor sites and acting as a "proton sponge", disrupting the endosome by osmolytic action. In preferred embodiments, the endosomolytic agent comprises a plurality of proton acceptor sites having pKas within the range of 4 to 7, which

endosomal lysing component is polycationic at pH 4. The present invention also contemplates the use of these endosomolytic agents as delivery agents by complexation with the desired compound to be delivered. Thus, the present invention also acts as a cell delivery system comprising an endosomolytic agent, a delivery agent, and a compound to be delivered.

PRIORITY INFORMATION

[0001] This application claims priority to the co-pending provisional application No. 60/075,272 entitled "Cell Delivery Compositions" filed on Feb. 19, 1998, which is incorporated in its entirety by reference.

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Time: 11:06:58

Application Number Information

Application Number: **09/251783** **Order This File** **Assignments**
Examiner Number: **77334 / LACOURCIERE, KAREN**
Filing or 371(c) Date: **02/17/1999**
Group Art Unit: **1635**
Effective Date: **02/17/1999**
Class/Subclass: **435/006.000**
Application Received: **02/17/1999**
Lost Case: **NO**
Pat. Num./Pub. Num: **6692911/20010006817**
Interference Number:
Issue Date: **02/17/2004**
Unmatched Petition: **NO**
Date of Abandonment: **00/00/0000**
L&R Code: Secrecy Code:**1**
Attorney Docket Number: **0492611-0313**
Third Level Review: **NO**
Secrecy Order: **NO**
Status: **150 /PATENTED CASE**
Status Date: **01/29/2004**
Confirmation Number: **3705**
Oral Hearing: **NO**
Title of Invention: **CELL DELIVERY COMPOSITIONS**

Bar Code	PALM Location	Location Date	Charge to Loc	Charge to Name	Employee Name	Location
09251783	9200	03/31/2004	No Charge to Location	No Charge to Name	BOADU,NANA	

Appln Info | Contents | Petition Info | Atty/Agent Info | Continuity Data | Foreign Data | Inv

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PCT / [ ] / [ ] Search **or PG PUBS #** [ ] Search
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L10: Entry 31 of 43 File: USPT Oct 16, 2001

DOCUMENT-IDENTIFIER: US 6303378 B1
TITLE: Methods for preparing polynucleotide transfection complexes

Brief Summary Text (6):
Engineered viruses are commonly used to deliver genes to cells. Viral vectors are generally efficient in gene delivery but have certain drawbacks, for example stimulation of an immune response when delivered in vivo. As a result, therefore, a number of non-viral nucleic acid delivery systems have been and continue to be developed. Thus, for example, cationic lipids are commonly used for mediating nucleic acid delivery to cells. See, for example, U.S. Pat. No. 5,264,618, which describes techniques for using lipid carriers, including the preparation of liposomes and pharmaceutical compositions and the use of such compositions in clinical situations. Other non-viral gene delivery systems likewise involve positively-charged carrier molecules, for example, peptides such as poly-L-lysine, polyhistidine, polyarginine, or synthetic polymers such as polyethylimine and polyvinylpyrrolidone.

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L16: Entry 14 of 15 File: USPT Nov 2, 1999

DOCUMENT-IDENTIFIER: US 5977083 A
TITLE: Method for using polynucleotides, oligonucleotides and derivatives thereof to treat various disease states

Detailed Description Text (275):
This process is superior to present viral vector directed gene therapy and would also enable competitive inhibition of proviral integration, and/or dislocation of the integrated pro-virus. Cellular uptake dynamics would directly define the anti-viral and genetic modulatory capacities of each respective nucleotide. Nucleic acid derivatives having chemical modifications are as described previously (e.g., nucleotides conjugated with poly(L-lysine) or which is modified by, for example, the addition of amino acids such as lysine, histidine and arginine, the addition of optimum concentrations of folate and/or biotin, the addition of the optimum ratios of metals and ions including zinc, manganese and iodine, by the addition of 5'-polyalkyl moieties, cholesterol, vitamin E, 1-2-di-0-hexadecyl-3-glyceryl and other lipophilic moieties and/or modified by the replacement of phosphodiester bonds with phosphothiotate bonds) and combination nucleic acids would be employed.

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L21: Entry 39 of 68 File: PGPB Jun 27, 2002

DOCUMENT-IDENTIFIER: US 20020082237 A1
TITLE: Cationic polymers and lipids for the delivery of nucleic acids

Detail Description Paragraph:
[0032] The cationic component used in the presently described cationic lipids and polymers may be monovalent, divalent, multivalent, or preferably polyvalent (i.e., polycationic). Examples of monovalent cations capable of associating with DNA include primary amines, including, but not limited to methylamine, ethylamine, etc.), and multivalent amines such as, but not limited to, spermine, spermidine, pentaethylenehexamine, diethylene triamine, pentamethylenehexamine, pentapropylenehexamine. The cationic component is preferably biocompatible or biotolerable. The cationic component may comprise any of a variety of chemical groups that retain a positive charge between pH 5 through pH 8 including, but not limited to, amino groups (or oligo or poly amines), e.g., spermine, spermidine, pentaethylehehexamine (PEHA), diethylene triamine, pentamethylenehexamine, pentapropylenehexamine, etc.), amide groups, amidine groups, positively charged amino acids (e.g., lysine, arginine, and histidine), imidazole groups, guanidinium groups, or mixtures and derivatives thereof.

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L21: Entry 59 of 68 File: USPT Nov 6, 2001

DOCUMENT-IDENTIFIER: US 6312727 B1
TITLE: Delivery of nucleic acid materials

Detailed Description Text (147):
Complexes can self-assemble between DNA and cationic polymers which are pH-responsive over the endosomal range, such as poly(ethylene imine). These are attractive polymers for DNA complexation since they possess good ability to transfect cells, perhaps by the mechanism described as the "Proton Sponge hypothesis" (Behr, Chimica 51, 34, 1997). However it is hard to define precisely their degree of ionisation at neutral pH, and therefore they should be used at weight ratios determined experimentally to mediate efficient complex formation. In this example, such a pH-responsive polymer was prepared by partial substitution of poly(L-lysine) with L-histidine. It is important that such polymers retain a significant component of reactive (primary or secondary) amino groups if surface modification is to be achieved using polymers bearing reactive esters. In this example the histidinylated poly(lysine) was allowed to self-assemble with DNA and the resulting particles were stabilised by surface modification using a hydrophilic polymer bearing pendant reactive esters. The hydrophilic polymer used was formed from alternating blocks of poly(ethylene glycol) and tripeptides, designed to introduce proteolytic degradability into the polymer backbone.

Detailed Description Text (172):
11.4 Self Assembly of Complexes Between DNA and Partially Histidine-Substituted poly(L-lysine), and Subsequent Stabilisation by Surface Modification Using pEG-peptide-ONp Repeating Polymer.

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